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INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

APPLICANT(S)

Martin Winn, et al.

FILING DATE

August 31, 2000

GROUP

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(Use several sheets if necessary)

(37 CFR 1.98 (b))

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		PATENT NUMBER	ISSUE DATE	INVENTOR	CLASS	SUB CLASS	FILING DATE
[Signature]	A1	3,342,833	09/19/67	Fremery et al.			
	A2	3,719,667	03/06/73	Gutowski			
	A3	3,840,556	10/08/74	Kukolja			
	A4	4,132,709	02/02/79	Santrouch et al.			
	A5	4,216,218	08/05/80	Ehrogott et al.			
	A6	4,340,715	07/20/82	Grounder et al.			
	A7	5,482,960	01/09/96	Berryman et al.			
	A8	5,668,164	09/16/97	Ma et al.			
	A9	5,998,468	12/07/99	Cheng et al.			
	A10	6,017,951	01/25/00	Patt et al.			
	A11	6,048,893	04/11/00	Smith et al.			

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION

		DOCUMENT NUMBER	PUBLIC- ATION DATE	COUNTRY OR PATENT OFFICE	CLASS	SUB CLASS	TRANS- LATION YES NO
[Signature]	B1	0 439 444	07/31/91	EP			
	B2	2,275,926	09/14/94	GB			
	B3	93/08799	05/13/93	PCT			
	B4	94/02474	02/03/94	PCT			
	B5	94/14434	07/07/94	PCT			
	B6	95/04534	02/16/95	PCT			
	B7	95/05372	02/23/95	PCT			
	B8	95/05376	02/23/95	PCT			
	B9	95/33748	12/14/95	PCT			
	B10	95/33752	12/14/95	PCT			
	B11	95/35107	12/28/95	PCT			
	B12	96/06095	02/25/96	PCT			
	B13	97/30046	08/21/97	PCT			

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

[Signature]	C1	Aktan et al., BQ-123, A Specific Endothelin (ETA) Receptor Antagonist, Prevents Ischemia-reperfusion Injury in Kidney Transplantation, <i>Transplant Int</i> , Vol. 9, 1996, pp. 201-207.
	C2	Benigni et al., "A Specific Endothelin Subtype A Receptor Antagonist Protects Against Injury in Renal Disease Progression", <i>Kidney International</i> , Vol. 44, 1993, pp. 440-444.
	C3	Berliner et al., <i>Journal of the American Chemical Society</i> , Vol. 72, 1950, pp. 222-227
	C4	Berridge et al., "Lithium Amplifies Agonist-dependent Phosphatidylinositol Responses in Brain and Salivary Glands", <i>Biochem. J.</i> , Vol. 206, 1982, pp. 587-595.
	C5	Bhagwat, S., "Synthesis of Enantiomerically Pure Pyrrolidinones as Endothelin Receptor Antagonists", <i>Tetrahedron Letters</i> , 37(27), 1996, pp. 4627-4630.
	C6	Bobik et al., "Growth Factor Activity of Endothelin on Vascular Smooth Muscle", <i>American Journal of Physiology</i> , Vol. 258, 1990, pp. C408-C415.



DATE: 02/20/01

SHEET 2 of 4

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

125	C7	Bonvallet et al., <i>American Journal of Physiology</i> , Vol. 266, 1994, pp. H1327-H1331.
	C8	Borch et al., "The Cyanohydrinborate Anion as a Selective Reducing Agent", <i>J. Am. Chem. Soc.</i> , Vol. 93, No. 12, 1971, pp. 2897-2904.
	C9	Bourguignon et al., <i>Canadian Journal of Chemistry</i> , Vol. 63, 1985, pp. 2354-2361.
	C10	Bowman, <i>J. Chem. Soc.</i> , 1950, pp. 1346-1349.
	C11	Bram et al., <i>Bull. Chem. Soc. France</i> , 1964, pp. 945-951.
	C12	Bredereck et al., <i>Chem. Berichte</i> , Vol. 97, 1964, pp. 3397-3406.
	C13	Brintzinger et al., <i>Chem. Berichte</i> , Vol. 85, 1952, pp. 455-457.
	C14	Bunchman et al., "Smooth Muscle Cell Proliferation by Conditioned Media from Cyclosporine-Treated Endothelial Cells: A Role of Endothelin", <i>Transplantation Proceedings</i> , Vol. 23, No. 1, 1991, pp. 967-968.
	C15	Bunting et al., <i>J. Am. Chem. Soc.</i> , Vol. 115, 1993, pp. 11705-11715.
	C16	Cahiez et al., Copper-Catalyzed Conjugate Addition of Organomagnesium Reagents to α , β -Ethylenic Esters: A Simple High Yield Procedure, <i>Tetrahedron Letters</i> , Vol. 31, No. 51, 1990, pp. 7425-7428.
	C17	<i>Chemical Abstract</i> , Vol. 74, No. 9, 1971, p. 304.
	C18	<i>Chemical Abstract</i> , Vol. 119, No. 21, 1993, p. 999.
	C19	Chobanian et al., Antiatherogenic Effect of Captopril in the Watanabe Heritable Hyperlipidemic Rabbit, <i>Hypertension</i> , Vol. 15, No. 3, 1990, pp. 327-331.
	C20	Clozel et al., Pathophysiological Role of Endothelin Revealed by the First Orally Active Endothelin Receptor Antagonist, <i>Nature</i> , Vol. 365, 1993, pp. 759-761.
	C21	Corey et al., <i>Tetrahedron Letters</i> , Vol. 36, 1972, pp. 3769-3772.
	C22	Cottrell et al., <i>J. Chem. Soc., Perkin Trans. 1</i> , Vol. 5, 1991, pp. 1091-1097.
	C23	Craig et al., "Modern Pharmacology, Third Edition", LITTLE, BROWN AND COMPANY, BOSTON, US, page 33, column 2 - page 35, column 1
	C24	Ferro et al., The Clinical Potential of Endothelin Receptor Antagonists in Cardiovascular Medicine, <i>Drugs</i> , Vol. 51, No. 1, 1996, pp. 12-27.
	C25	Foegh et al., "Inhibition of Coronary Artery Transplant Atherosclerosis in Rabbits with Angiopeptin, an Octapeptide", <i>Atherosclerosis</i> , Vol. 78, 1989, pp. 229-236.
	C26	Fung et al., "Nonpeptide Renin Inhibitors Employing a Novel 3-Aza (or oxa)-2,4-dialkyl Glutaric Acid Moiety as a P2/P3 Amide Bond Replacement", <i>J. Med. Chem.</i> , Vol. 35, No. 10, 1992, pp. 1722-1734.
	C27	Ge, et al., <i>Yaoxue Xuebao</i> , <u>20</u> 427-432 (1985)
	C28	Gershon et al., <i>J. Heterocyclic Chem.</i> , Vol. 24, 1987, pp. 205-209.
	C29	Greene et al., "Protective Groups in Organic Synthesis", 2 nd Ed., 1991, pp. 152-186.
	C30	Gupton et al., <i>Synthetic Communications</i> , Vol. 12, No. 1, 1982, pp. 35-41.
	C31	Hara et al., Amelioration of Brain Damage after Focal Ischemia in the Rat by a Novel Inhibitor of Lipid Peroxidation, <i>European J. Pharmacol.</i> , Vol. 197, 1991, pp. 75-82.
	C32	Hatt, <i>Journal of the Chemical Society</i> , Vol. 132, 1929, pp. 1623-1632.
	C33	Heistad et al., <i>Circulation Research</i> , Vol. 54, No. 6, 1984, pp. 711-718.
	C34	Higuchi et al., "Pro-drugs as Novel Delivery Systems", A.C.S. Symposium Series, <i>American Chemical Society</i> , Vol. 14, (1975).
	C35	Hirata et al., <i>Biochem. Biophys. Res. Commun.</i> , Vol. 154, No. 3, 1988, pp. 868-875.
126	C36	Hogaboam et al., An Orally Active Non-selective Endothelin Receptor Antagonist, Bosentan, Markedly Reduces Injury in a Rat Model of Colitis, <i>European J. Pharmacol.</i> , Vol. 309, 1996, pp. 261-269.



DATE: 02/20/01

SHEET 3 of 4

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

65	C37	Hoshino et al., "A Convenient Preparation of Certain N,N-Dialkylcarbamoyl Chlorides", <i>Synthetic Communications</i> , Vol. 17, No. 16, 1987, pp. 1887-1892.
	C38	Hudlicky et al., <i>Synthetic Communications</i> , Vol. 16, No. 2, 1986, pp. 169-182.
	C39	Imbriaco et al., <i>Clinical Cancer Research</i> , Vol. 4, 1998, pp. 1765-1772.
	C40	Ishida et al., <i>Biochem. Pharmacol.</i> , Vol. 44, No. 7, 1992, pp. 1431-1436.
	C41	Itoh et al., <i>Biochemical and Biophysical Research Communications</i> , Vol. 195, No. 2, 1993, pp. 969-975.
	C42	Itoh et al., <i>FEBS Letters</i> , Vol. 231, No. 2, 1988, pp. 440-444.
	C43	"IUPAC 1974 Recommendations for Section E, Fundamental Stereochemistry", <i>Pure Appl. Chem.</i> , Vol. 45, pp. 13-30 (1976).
	C44	Jae, et al., "Pyrrolidine-3-carboxylic acids as Endothelin Antagonists. 2. Sulfonamide-Based ETA-ETB Mixed Antagonists." <i>JOURNAL OF MEDICINAL CHEMISTRY</i> , Vol. 40, No. 20, 1997, pp. 3217-3227.
	C45	Kaldor et al., "A Mild, Osmium Tetraoxide-Catalyzed Method for the Oxidation of Sulfides to Sulfones", <i>Tetrahedron Letters</i> , Vol. 32, No. 38, 1991, pp. 5043-5046.
	C46	Kanemasa et al., "Nonstabilized Azomethine Ylides Generated by Decarboxylative Condensation of α -Amino Acids. Structural Variation, Reactivity, and Stereoselectivity", <i>Bull. Chem. Soc. Of Japan</i> , Vol. 62, No. 6, 1989, pp. 1960-1968.
	C47	Klemm et al., "Endothelin 1 Mediates <i>ex vivo</i> Coronary Vasoconstriction Caused by Exogenous and Endogenous Cytokines", <i>Proc. Natl. Acad. Sci.</i> , Vol. 92, 1995, pp. 2691-2695.
	C48	Kon et al., "Glomerular Actions of Endothelin In Vivo", <i>J. Clin. Invest.</i> , Vol. 83, 1989, pp. 1762-1767.
	C49	Kon et al., "Role of Endothelin in Cyclosporine-induced Glomerular Dysfunction", <i>Kidney International</i> , Vol. 37, 1990, pp. 1487-1491.
	C50	Krapcho et al., <i>Organic Syntheses</i> , Vol. 47, 1967, pp. 20-23.
	C51	Margulies et al., <i>Circulation</i> , Vol. 82, No. 6, 1990, pp. 2226-2230.
	C52	Matsumura et al., <i>European Journal of Pharmacology</i> , Vol. 185, 1990, pp. 103-106.
	C53	Matsumura et al., <i>Life Sciences</i> , Vol. 49, 1991, pp. 841-848.
	C54	McMurdo et al., <i>European Journal of Pharmacology</i> , Vol. 259, 1994, pp. 51-55.
	C55	Nakagomi et al., <i>J. Neurosurg.</i> , Vol. 66, 1987, pp. 915-923.
	C56	Nelson et al., <i>Nature Medicine</i> , Vol. 1, No. 9, 1995, pp. 944-949.
	C57	Nelson et al., <i>Urology</i> , Vol. 53, No. 5, 1999, pp. 1063-1069.
	C58	Potvin et al., <i>Canadian Journal of Physiol. And Pharmacol.</i> , Vol. 67, 1989, pp. 1213-1218.
	C59	Prescott, ed., <i>Methods in Cell Biology</i> , Vol. XIV, pp. 33 et seq., Academic Press, New York, NY (1976).
	C60	Rahman, <i>Indian J. Chem.</i> , Sec B, 19B 828-830 (1980)
	C61	Rapoport et al., <i>J. Org. Chem.</i> , 1986, Vol. 51, pp. 5106-5110.
	C62	Roche, E.B. Editor, "Bioreversible Carriers in Drug Design: Theory and Application", pp. 13-21, Pergamon Press, New York (1987).
	C63	Seydal et al., "ChemiStruktur und biologische Aktivitat von Wirkstoffen." VERLAG CHEMIE, WEINHEIM, DE, 1979, page 124, paragraph 2 -page 126, paragraph 2.
	C64	Shichiri et al., <i>J. Clin. Invest.</i> , Vol. 87, 1991, pp. 1867-1871.
	C65	Streitwieser et al., <i>Tetrahedron Letters</i> , Vol. 42, 1971, pp. 3927-3930.
	C66	Takahashi et al., <i>Clinical Science</i> , Vol 79, 1990, pp. 619-623.
19	C67	Tasker, et al., "Potent and Selective Non-Benzodioxole Containing Endothelin- A Receptor Antagonists" 1997, <i>JOURNAL OF MEDICINAL CHEMISTRY</i> .
	C68	Taylor et al., <i>J. Org. Chem.</i> , Vol. 54, 1989, pp. 3618-3624.



DATE: 02/20/01

SHEET 4 of 4

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

C69	Topliss, "Quantitative Structure-Activity Relationships of Drugs", ACADEMIC PRESS, NEW YORK, page 453, paragraph 2 - page 456, paragraph 2
C70	Isuge, et al. Chemistry Letters, 801-804 (1984)
C71	Isuge, et al. Bull. Chem. Soc. Jpn 59 2537 (1986)
C72	Isuge et al., Chemistry Letters, 1983, pp. 1131-1134.
C73	Isuge et al., J. Org. Chem., 1987, Vol. 52, pp. 2523-2530.
C74	U.S. Department of Health and Human Services. "Management of Cancer Pain Clinical Guideline Number 9." AHCPR Publication No. 94-0592: March 1994.
C75	Vilsmair et al., Liebigs Ann. Chem., 1980, pp. 1055-1063.
C76	Wallace et al., Am. J. Physiol., 1989, Vol. 256, pp. G661-G666.
C77	Watanabe et al., Nature, Vol. 344, 1990, pg. 114.
C78	Weaver et al., J. Amer. Chem. Soc., Vol. 69, 1947, pp. 515-516.
C79	Wenkert et al., J. Org. Chem., Vol. 48, 1983, pp. 5006-5009.
C80	Winn, et al., "2.4-Diarylpiperidine-3-carboxylic Acids-Potent EtA Selective Endothelin Receptor Antagonists. 1. Discovery of A-127722.", Journal of Medicinal Chemistry, Vol. 39, No. 5, 1996, pp. 1039-1048.
C81	Wu-wong et al., Life Sciences, Vol. 58, No. 21, 1996, pp. 1839-1847.
C82	Yamagishi et al., Biochem. Biophys. Res. Comm., Vol. 191, No. 3, 1993, pp. 840-846.
C83	Yamamoto et al., J. Pharmacol. Exp. Therapeutics, Vol. 271, 1994, pp. 156-163.
C84	Yanagisawa et al., Nature, Vol. 332, 1988, pp. 411-415.
C85	U. S. Patent Application Serial No. 09/634,661, filed August 7, 2000.
C86	U. S. Patent Application Serial No. 09/048,955, filed March 27, 1998.
C87	U. S. Patent Application Serial No. 08/794,506, filed February 4, 1997.
C88	U. S. Patent Application Serial No. 08/600,625, filed February 13, 1996.
C89	U. S. Patent Application Serial No. 08/497,998, filed August 2, 1995.
C90	U. S. Patent Application Serial No. 08/442,575, filed May 30, 1995.
C91	U. S. Patent Application Serial No. 08/334,717, filed November 4, 1994.
C92	U. S. Patent Application Serial No. 08/293,349, filed August 19, 1994.

EXAMINER

DATE CONSIDERED

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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